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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/009,134	10/20/2002	Chandrasekhar Satishchandran	NUCL-001/01US 306512-2006	5538

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EXAMINER	
CHONG, KIMBERLY	
ART UNIT	PAPER NUMBER
1635	
MAIL DATE	DELIVERY MODE
02/09/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Advisory Action Before the Filing of an Appeal Brief	**Application No.** 10/009,134	**Applicant(s)** SATISHCHANDRAN ET AL.	
	Examiner KIMBERLY CHONG	**Art Unit** 1635	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 27 October 2008 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☐ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☐ The period for reply expires _____months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☒ The Notice of Appeal was filed on *27 October 2008*. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☐ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: _____.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
12. ☐ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). _____
13. ☐ Other: _____.

/Kimberly Chong/ AU1635

Continuation of 11. does NOT place the application in condition for allowance because: the clamed invention would be prima facie obvious to one of ordinary skill in the art at the time the invention was made as stated in the previous Office action. Applicant reiterates their arguments regarding Fire et al. not being enabling for inhibiting gene expression in mammalian cells and there being no reasonable expectation of success given the known PKR response obstacle for RNA interference. In response, as stated in the previous Office action, the fact that Fire et al. does not reduce to practice the invention does not mean the invention was not enabled. Applicants entire argument is drawn to the fact that Fire et al., although describing the use of dsRNA to mediate RNAi, is not enabled and that because of the PKR response using long dsRNA such as Fire et al. there would not have been a reasonable expectation of success. However Applicant has not addressed Examiners point regarding the fact that there are no manipulative differences or any structural differences in Applicants invention of mediating RNAi using long dsRNA as compared to the methods taught by Fire et al. and the fact that Applicants invention using long dsRNA have seemingly overcome the PKR problem they are arguing against. Applicant has merely reduced to practice the invention taught by Fire et al. Applicant's argue that the Examiner "entirely disregarded the statements made by Dr. McCallus with respect to the widely reported phenomenon of promoter interference", the Examiner has not provided any evidence to the contrary demonstrating the promoter interference is not a common problem and that given the declaration of Dr. McCallus and the teachings of Hull et al., the skilled artisan would have some doubts as to the success of efficient expression of multiple dsRNA. To the contrary, the assertions of Dr. McCallus as well as the evidence presented in the Hull et al. reference were addressed on page 7 of the previous Office action. As stated previously, the assertions by Dr. McCallus coupled with the teachings of Hull et al. were not convincing because Dr. McCallus nor Hull et al. provides any direct evidence against the use of multiple pol promoters, particulary pol III promoters. Hull et al. observed many aspects of regulation of expression of genes and even suggests this could be the actual tRNA gene itself (see page 1273, column 2). The statement pointed out by Applicant on pae 1273 of Hull et al. would lead one to conclude that pol III promoters may have different roles in regulation of surrounding genes and not necessarily promoter interference and the fact that Hull et al. state "it would not be suprising to find" means that Hull et al. was merely conjecturing a hypothesis and has not conclusively proven this statement. Applicant agues against the teachings of Heifetz et al. as not teaching expression of multiple dsRNA but merely teaching the expression of an antisense and sense strand and one cannot infer from that reference that a vector encoding multiple double stranded RNA molecules under the control of different promoters would be successful. This argument is not convincing because, Heifetz et al. teach the use of multiple promoters capable of expressing multiple nucleic acid sequences from the same vector and one would have expected success at being able to construct a single vector capable of expression multiple dsRNA. Thus the rejection of record is maintained.